UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/805,840	03/13/2001	Gregory R. Mundy	10274-034001	4957

26161 7590 07/30/2003

FISH & RICHARDSON PC
225 FRANKLIN ST
BOSTON, MA 02110

EXAMINER
HADDAD, MAHER M

ART UNIT	PAPER NUMBER
1644	18

DATE MAILED: 07/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/805,840	MUNDY ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

riod for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *5/6/03* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-41* is/are pending in the application.

4a) Of the above claim(s) *3,6-8,10-30 and 33* is/are withdrawn from consideration.

5)☒ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,5,9,31,32 and 34-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *16* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 5/6/03 (Paper No. 15), is acknowledged.

2. Claims 1-41 are pending.

3. Claims 3, 6-8 and 10-30 and 33 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention.

4. Claims1, 2, 4,5, 9, 31-32 and 34-41 are under consideration as they read on a method of treating multiple myeloma with alpha4-specific antibody.

5. The following new grounds of rejections are necessitated by the amendment filed on 5/6/03, paper No. 15.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 34-41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claims 34-41 are indefinite in the recitation of "HP1/2", "HP2/1", "HP2/4", "L25", "P4C2", "P4G9", " 21-6" and "21.6", respectively because its characteristics are not known. The use of "HP1/2", "HP2/1", "HP2/4", "L25", "P4C2", "P4G9", " 21-6" and "21.6" antibody homology as the sole means of identifying the claimed antibody renders the claim indefinite because "HP1/2", "HP2/1", "HP2/4", "L25", "P4C2", "P4G9", " 21-6" and "21.6" are merely a laboratory designation which does not clearly define the claimed product, since different laboratories may use the same laboratory designations to define completely distinct antibody homolog.

B. Claims 40 and 41 are indefinite because in the recitation of "21-6" and "21.6" because it is not clear which antibody is claimed. Is the antibody 21-6 or 21.6.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 34-41 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification disclosure does not enable one skilled in the art to practice the invention without an undue amount of experimentation.

It appears that the "HP1/2", "HP2/1", "HP2/4", "L25", "P4C2", "P4G9", " 21-6" and "21.6" antibodies are essential to practice the claimed invention. However the specification fails to teach how to make the specific antibodies. Applicant's attempt to incorporate "HP1/2", "HP2/1", "HP2/4", "L25", "P4C2", "P4G9", " 21-6" and "21.6" is considered improper.

The incorporation of essential material in the specification by reference to Sanchez-Madrid et al., (Eur. J. Immunol., 16:1343-1349, 1986), Hemler et al., (J. Biol. Chem., 262:11478-11485, 1987), Pulido et al., (J. Biol. Chem., 266(16), 10241-10245, 1991) (page 19, lines 5-10) and PCT/US95/01219 (page 23, lines 13-17) for "HP1/2", "HP2/1", "HP2/4", "L25", "P4C2", "P4G9", " 21-6" and "21.6" is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

The attempt to incorporate subject matter into this application by reference to Sanchez-Madrid et al., (Eur. J. Immunol., 16:1343-1349, 1986), Hemler et al., (J. Biol. Chem., 262:11478-11485, 1987), Pulido et al., (J. Biol. Chem., 266(16), 10241-10245, 1991) (page 19, lines 5-10) and PCT/US95/01219 (page 23, lines 13-17) for "HP1/2", "HP2/1", "HP2/4", "L25", "P4C2", "P4G9", " 21-6" and "21.6" is improper because an application for a patent when filed may incorporate "essential material" by reference to (1) a United States patent or (2) an allowed U.S. application, see MPEP 608.01(p),. "Essential material" is defined as that which is necessary to (1) support the claims, or (2) for adequate disclosure of the invention (35 U.S.C. 112). "Essential material" may not be incorporated by reference to (1) patents or applications published by foreign countries or regional patent offices, to (2) non-patent publications, to (3) a U.S. patent or application which itself incorporates "essential material" by reference or to (4) a foreign application. See In re Fouche, 169 USPQ 429; 439 F.2d 1237 (CCPA 1971).

Further, It is apparent that the antibodies "HP1/2", "HP2/1", "HP2/4", "L25", "P4C2", "P4G9", " 21-6" and "21.6" are essential and required to practice the claimed invention. As a required element, the hybridoma that secret the "HP1/2", "HP2/1", "HP2/4", "L25", "P4C2", "P4G9", " 21-6" and "21.6" must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If it is not so obtainable or available, the enablement requirements of 35 USC 112, a deposit of the hybridoma, which produces this antibody, may satisfy first paragraph. See 37 CFR 1.801-1.809.

If the deposits have been made under the terms of the Budapest Treaty, an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the hybridoma has been deposited under the Budapest Treaty and that the hybridoma will be irrevocably and without restriction or condition released to the public upon the issuance of a patent would satisfy the deposit requirement made herein. See 37 CFR 1.808. Further, the record must be clear that the deposit will be maintained in a public depository for a period of 30 years after the date of deposit or 5 years after the last request for a sample *or for the enforceable life of the patent whichever is longer*. See 37 CFR 1.806. If the deposit has not been made under the Budapest treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature much be made, stating that the deposit has been made at an acceptable depository and that the criteria set forth in 37 CFR 1.801-1.809, have been met.

If the deposits were made after the effective filing date of the application for a patent in the United States, a verified statement is required from a person in a position to corroborate that the hybridoma described in the specification as filed are the same as that deposited in the depository. Corroboration may take the form of a showing of a chain of custody from applicant to the depository coupled with corroboration that the deposit is identical to the biological material described in the specification and in the applicant's possession at the time the application was filed.

Further, amendment of the specification to disclose the date of deposit and the complete name and address of the depository (ATCC.10801 University Boulevard, Manassas, VA 20110-2209) is required as set forth in 37 C.F.R. 1.809(d).

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> *(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.*

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 1-2, 4, 5, 9, 31-32 and 34-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Van Zaanen et al (Br. J. Haematol. 102:783-90, August 1998) in view of Masellis-Smith et al (IDS Ref No. AJ and Lokhorst et al (Blood 84:2269-2277, 1994) and Owens *et al* (1994) for the same reasons set forth in the previous Office Action, paper No. 12, mailed 11/04/02.

Van Zaanen et al teach a method for treating multiple myeloma comprising administering chimaeric monoclonal anti-IL-6 antibodies (cMab) in multiple myeloma patients, the cMab was given in a dosage of 5-40 mg/d) (see the entire document and the abstract on page 783 in particular).

The Van Zaanen *et al* teaching differs from the claimed invention by not expressly disclosing to employ an antibody anti-alpha4 integrin antibody homolog or antigen binding fragment thereof in claim 1, wherein the composition is an alpha 4 integrin binding agent in claim 2, wherein the anti-alph4 integrin antibody homolog is an antibody homolog that antagonizes the interaction of VLA-4 with its alpha4 ligand in claim 4, where in the antibody homolog is selected from the group consisting of a human antibody, a chimeric antibody, and a humanized antibody in claims 5, wherein the antibody homolog is administered at a dose so as to provide from about 0.1 to about 20 mg/Kg body weight in claim 9, wherein the antibody is a human or humanized in claims 31-32 and wherein the VLA-4 antibody homolog is an HP2/1 antibody homolog in claim 35.

Masellis-Smith et al teach function-blocking monoclonal antibodies such as mAbs (HP2/1) against very late antigen 4 that inhibit the CD19+ multiple myelom blood B cell interaction with BM fibroblasts. Furthermore, Masellis-Smith et al teach that the alpha4beta7 ligand is mediated MM blood B cell adhesion (see the entire document and abstract page 930 in particular).

Lokhorst *et a*l teach monoclonal antibodies directed to the α4-integrin (VLA-4) that inhibit binding of purified myeloma cells to long term bone marrow cultures (LTBMC) from patients with multiple myeloma. Furthermore, the antibodies to VLA-4 inhibited the induced IL-6 secreation. Furthermore, Lokhorst *et al* teach that the intimate cell-cell contact is a prerequisite for IL-6 induction and the physical separation of plasma cells and LTBMC by mechanical means such as monoclaonal antibodies to VLA-4 which is involved in the adhesion process, inhibit the induction of IL-6 production by LTBMC. (entire document and abstract page 2269, and page 2276, left column 2nd paragraph in particular).

Owens *et al* teach the modification of murine antibodies such as a chimeric antibody, a single chain antibody, a Fab fragment, a F(ab')$_2$ fragment or a humanized antibody antibodies. Owens *et al* further teach humanized antibodies use in therapy of human diseases or disorders, since the human or humanized antibodies are much less likely to induce an immune response. Also,

antibody fragments are the reagents of choice for some clinical applications, and the chimeric antibodies offers the ability to mediate antigen-dependent cytotoxicity and complement – dependent cytotoxcity (see the entire document).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the antibody taught by the Van Zaanen *et al* with the antibody that specifically binds the α4 integrin taught by Masellis-Smith *et al* or Lokhorst *et al*., using human antibody, chimeric antibody, a humanized antibody and fragments thereof as taught by Owens *et al* in a method of treating multiple myeloma (MM).

One of ordinary skill in the art at the time the invention was made would have been motivated to substitue the anti-IL-6 antibodies with anti-α4 antibodies in a method of treating MM because antibodies against alpha4 integrin inhibit cell-cell contact which is a prerequisite for IL-6 induction as taught by Lokhorst *et al* and because antibodies against alpha4 integrin inhibit the adhesion of alpha4beta7 integrin of B cells from MM patients with its ligand on the bone marrow (BM) fibroblast and hence prevent extravasation into the BM. Further, the humanized antibodies are much less likely to induce an immune response and because the antibody fragments are the reagents of choice for some clinical applications and the chimaeric antibodies offers the ability to mediate antigen-dependent cytotoxicity and complement-dependent cytotoxcity as taught by Owens *et al*.

Claim 9 is included because the determination of the optimal dosage of treatment is well within the purview of one of ordinary skill in the art at the time the invention was made and lends no patentable import to the claimed invention. Further, one of ordinary skill in the art would have been motivated to modify and narrow the dosage of the antibodies because all these dosages are overlap with the dosages taught by the Van Zaanen *et al* to treat multiple myeloma.

Claims 34-39 are included because Masellis-Smith et al teach monoclonal antibodies such as mAbs (HP2/1), which is considered as antibody homolog of "HP1/2", "HP2/4", "L25", "P4C2", "P4G9".

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expection of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments, filed 5/6/03 (Paper No. 15), have been fully considered, but have not been found convincing.

Applicant submits that the Declaration of Dr. Gregory Mundy under 37 CRF 1.131, which states that Applicants conceived the claimed invention prior to August 18, 1998, and diligently reduced the invention to practice thereafter. Applicant argues that Van Zaanen is not available as prior art against the present claims.

However, the Mundy Declaration under 37 CFR 1.132 filed 5/6/03 is insufficient to overcome the rejection of claims 1-2, 4, 5 and 9 based upon 35 U.S.C. 103 as set forth in the last Office action because: 1) the Mundy Declaration is not signed by all inventors (i.e. Toshiyuki Yoneda), 2) Applicant has not provided documentary evidence such as notebook pages and photographs as evidence of conception, diligence and reduction to practice. The Mundy declaration for the most part consists of vague and general statements in the broadest terms, and 3) it is not clear for the Mundy Declaration as to when the reduction to practice occurred prior or after the Van Zaanen et al reference date.

12. Claims 34-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Van Zaanen et al (Br. J. Haematol. 102:783-90, August 1998) in view of Masellis-Smith et al (IDS Ref No. AJ and Lokhorst et al (Blood 84:2269-2277, 1994) and Owens *et al* as applied to claims 1-2, 4, 5, 9 and 31-32 above, and further in view of US Patent No. 5,932,214 A and Kamata et al (Biochem J. 305:945-951, 1995).

The teachings of Van Zaanen et al, Masellis-Smith et al, and Owens *et al* have been discussed, supra.

The claimed invention differs from the reference teachings only by the recitation of HP1/2, HP2/4, L25, P4C2 and P4G9 in claims 34 and 36-39, respectively.

The `214 patent teaches that monoclonal antibodies such as HP1/2, HP2/1, HP2/4, L25, P4C2 that are capable of recognizing the x chain of VLA-4, which are useful for inhibiting the migration of VLA-4 expressing leukocytes to inflammatory mediators and cytokines by leukocytes already recruited to IBF tissue may be blocked by anti-VLA-4 antibodies that prevent some form of VCAM-1 mediated signal transduction (col., 4, lines 54-67 in particular).

Kamata et al teach that the anti-alpha 4 functional blocking antibodies such as P4C2 (epitope B2) and P4G9 (within resitues 1-52) (see abstract in particular).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the anti-alpha4 antibody taught by Masellis-Smith et al with mAb HP1/2, HP2/4, L25, P4C2, P4G9 taught by the `124 patent and Kamata et al in a method for treating MM as taught by Van Zaanen *et al*.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because antibodies are functional blocking as taught by Kamata et al and such antibodies are useful for in vivo use as taught by `241 patent.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

13. The following new ground of rejections.

14. Claims 1-2, 4, 5, 9, 31-32 and 34-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 6,495,525 in view of U.S Patent No. 5,932,214 and Kamata et al .

The `525 patent teaches a method for treating multiple myeloma in a mammal comprising administering to a compounds which are capable of inhibiting VLA-4 mediated cell adhesion by inhibiting the binding of ligands to that receptor such as oMePUPA-V (see patented claim 9, col., 30, and col., 4, line 21-40 in particular). The `525 patent further teaches anti-VLA-4 monoclonal antibodies which have been shown to inhibit VLA-4 dependent adhesion interactions both in vitro and in vivo (see col., lines 57-58 in particular). Additionally, the `525 patent teaches that the compounds of the invention are inhibitors of VLA-4 integrin thereby blocking the binding of VLA-4 to its various ligand, such as VCAM-1 and regions of fibronectin. These compounds are useful in inhibiting cell adhesion processes, including cell activation, migration, proliferation and differentiation. These compounds are useful for inhibition, prevention and suppression of VLA-4-mediated cell adhesion and pathologies associated with that adhesion such as multiple myeloma (col., 2, line 64 through col., 3, line 21 in particular). Finally, the `525 patent teaches the composition is employed in dosage range from about 0.001-25 mg/kg (see col., 10, lines 60-63 inparticular).

The claimed invention differs from the reference teachings only by the recitation of HP1/2, HP2/1, HP2/4, L25, P4C2 and P4G9 in claims 34-39, respectively.

The `214 patent teaches that monoclonal antibodies such as HP1/2, HP2/1, HP2/4, L25, P4C2 that are capable of recognizing the x chain of VLA-4, which are useful for inhibiting the migration of VLA-4 expressing leukocytes to inflammatory mediators and cytokines by leukocytes already recruited to IBF tissue may be blocked by anti-VLA-4 antibodies that prevent some form of VCAM-1 mediated signal transduction (col., 4, lines 54-67 in particular). The `214 patent further teaches that the antibodies of the invention can CDR-grafted antibodies or humanized antibodies, a human antibody, VLA-4 binding fragments (see col., 6, lines 25-46 in particular).

Kamata et al teach that the anti-alpha 4 functional blocking antibodies such as P4C2 (epitope B2) and P4G9 (within resitues 1-52) (see abstract in particular).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the compound which are capable of inhibiting VLA-4 mediated cell adhesion by inhibiting the binding of ligands to that receptor such as oMePUPA-V taught by the `525 patent with anti-VLA-4 monoclonal antibodies have been shown to inhibit VLA-4-dependent adhesion interactions both in vitro and in vivo taught by the `525 patent in in a method for treating MM as taught by the `525 patent and further substitute the anti-VLA-4 monoclonal antibody taught by the `525 patent with amAb HP1/2, HP2/4, L25, P4C2, P4G9 taught by the `124 patent and Kamata et al.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because the `525 suggested the substitution implicitly because the compounds of the invention are inhibitors of VLA-4 integrin thereby blocking the binding of VLA-4 to its various ligand, such as VCAM-1 and regions of fibronectin such is antibodies to VLA-4. These compounds are useful in inhibiting cell adhesion processes, including cell activation, migration, proliferation and differentiation. Further, the Kamata's et al antibodies are functional blocking and the `241 patent antibodies are useful for in vivo use.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

15. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

16. Claims 1-2, 4-5 and 9 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 1-2, 4-5 and 11 of copending Application No. 09/943,659. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Applicant indicates that once the present application deemed allowable, Applicant will address this rejection by canceling or amending the relevant claims of U.S.S. 09/943,659.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

17. Claims 1-2, 4-5, 9 and 31-32 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-2, 4-5, 9, 11-12, 17-8, 20-21, 25, 27, 34-35, 37 and 44 of copending Application No.10/086,217. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1-2, 4-5, 9, 11-12 of Application `217 are drawn to the same method of treatment using the same composition comprising anti-alpha-4 antibodies. Further, while the preamble of the conflicting claims 17-8, 20-21, 25, 27, 34-35, 37 and 44 are different, the same product is used in the method with same method steps and patient populations, therefore the practice of the invention of `217 would necessarily result in the practice of the instant invention and vice versa.

Claim 12 of application `217 is included because the term "comprising" in the instant applicant opens up the composition to other unrecited materials such as those recited in claim 12 of application `217.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

18. Claim 34-39 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-2, 4-5, 9, 11-12, 17-8, 20-21, 25, 27, 34-35, 37 and 44 of copending Application No. 10/086,217 in view of U.S. Patent No. U.S Patent No. 5,932,214 and Kamata et al.

The teachings of claims 1-2, 4-5, 9, 11-12, 17-8, 20-21, 25, 27, 34-35, 37 and 44 of Application `217, have been discussed, supra.

The claimed invention differs from the reference teachings only by the recitation of HP1/2, HP2/1, HP2/4, L25, P4C2 and P4G9 in claims 34-39, respectively.

The teachings of `214 patent and Kamata et al reference have been discussed, supra.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the antibody homolog that antagonizes the interaction of both VLA-4 with its ligand taught by the `217 application with HP1/2, HP2/1, HP2/4, L25, P4C2, P4G9 taught by the `124 patent and Kamata et al.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because the Kamata's et al antibodies are functional blocking antibodies and the `241 patent antibodies are useful for in vivo use.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

This is a provisional obviousness-type double patenting rejection.

19. No claim allowed

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad, whose telephone number is (703) 306-3472. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Maher Haddad, Ph.D.
Patent Examiner
Technology Center 1600
July 28, 2003

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600